REMARKS

Claim 37 has been amended to recite that an effective amount of isovaleramide is administered to a patient suffering from a convulsive disorder, wherein the convulsive disorder is selected from the group consisting of simple partial seizures, complex partial seizures, generalized tonic-clonic seizures, secondarily generalized seizures, status epilepticus, and trauma-induced seizures. Support for the amendment is found in the as-filed specification at (at least) p. 9, lines 18-22 and p. 10, lines 3-7. Claim 39 has been amended to recite that an effective amount of isovaleramide is administered to a patient suffering from headaches. Support for this amendment is found in the as-filed specification at (at least) p. 12, lines 2-8.

The Office Action mailed April 28, 2005, has been received and reviewed. Claims 37 and 39 are currently pending in the application. Claims 37 and 39 stand rejected. Applicants have amended claims 37 and 39 and respectfully request reconsideration of the application as amended herein.

35 U.S.C. § 103(a) Obviousness Rejection

Obviousness Rejection Based on United States Patent No. 5,506,268 to Balandrin *et al.* in view of Dorland's Medical Dictionary 27th Ed. p. 379

Claim 37 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over United States Patent No. 5,506,268 to Balandrin *et al.* ("Balandrin") in view of Dorland's Medical Dictionary, 27th Ed. p. 379 ("Dorland"). Applicants respectfully traverse this rejection, as hereinafter set forth.

M.P.E.P. 706.02(j) sets forth the standard for an obviousness rejection:

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

The obviousness rejection of claim 37 is improper because the cited references do not teach or suggest all of the claim limitations, do not provide a reasonable expectation of success, and do not provide a motivation to produce the claimed invention.

Balandrin teaches using isovaleramide as an anxiolytic or sedative agent in humans. Balandrin at column 1, lines 9-11. Depending on the dose administered, the isovaleramide acts as a mild anxiolytic or mild sedative. *Id.* at column 5, lines 46-48. In addition to its sedative and anxiolytic activity, isovaleramide is administered to hyperexcitable children, premenstrual patients, and substance abuse patients. *Id.* at column 7, lines 25-30. Balandrin also teaches that extracts of valerian have been used as sedatives or antispasmodics. *Id.* at column 1, lines 53-61. Active components of the valerian extracts have not been identified or the effects of the active components characterized. *Id.* at column 2, lines 15-21. Isovaleramide exhibits hypnotic activity when administered to experimental animals in high doses but is not clinically effective as a hypnotic. *Id.* at column 3, lines 3-9. While Balandrin teaches that valproic acid and valpromide are used as antiepileptic agents, Balandrin explicitly states that isovaleramide has no anticonvulsant properties. *Id.* at column 4, lines 60-65. Balandrin also explicitly states "that there are no clearly discernible structure-function relationships which permit predictability of compounds which will affect the central nervous system in the experimentally distinguishable outcomes described herein below." *Id.* at column 4, line 66 through column 5, line 3.

Dorland teaches that a convulsion is "a violent involuntary contraction or series of contractions of the voluntary muscles."

As amended, claim 37 recites a method of treating convulsions in a patient. The method comprises administering an effective amount of isovaleramide to a patient suffering from a convulsive disorder, wherein the convulsive disorder is selected from the group consisting of simple partial seizures, complex partial seizures, generalized tonic-clonic seizures, secondarily generalized seizures, status epilepticus, and trauma-induced seizures.

The cited references do not teach or suggest the limitation of "administering an effective amount of isovaleramide to a patient suffering from a convulsive disorder, wherein the convulsive disorder is selected from the group consisting of simple partial seizures, complex partial seizures, generalized tonic-clonic seizures, secondarily generalized seizures, status epilepticus, and trauma-induced seizures." As acknowledged by the Examiner, "Balandrin does

not specifically teach methods of treating convulsions." Office Action of April 28, 2005, p. 3. Applicants respectfully submit that nothing in Balandrin teaches or suggests administering isovaleramide to a patient suffering from a convulsive disorder. Rather, Balandrin is limited to teaching that isovaleramide is administered as an anxiolytic or sedative. Therefore, Balandrin necessarily does not teach or suggest that the convulsive disorder is selected from the group consisting of simple partial seizures, complex partial seizures, generalized tonic-clonic seizures, secondarily generalized seizures, status epilepticus, and trauma-induced seizures.

As evidence that Balandrin teaches this limitation, the Examiner presents an elaborate argument that attempts to equate spasms with a convulsion. *Id.* at p. 3-4. The Examiner states that "isovaleramide is prepared from extracts of *valeriana officinalis*, which has historically been used as sedative and antispasmodics" and that "the limitation of 'treating convulsions' is viewed to encompass any alleviation that lessens one or more spasms of muscles, including decreasing muscle tone." *Id.* at p. 3. However, contrary to the Examiner's assertions, nothing in Balandrin teaches or suggests that isovaleramide has antispasmodic effects. While Balandrin teaches that valerian extracts have antispasmodic effects, it is improper for the Examiner to rely on this teaching in support of the assertion that isovaleramide has antispasmodic effects, especially since Balandrin teaches that the active components in the valerian extracts have not been identified, nor have the effects of the active components been characterized.

Furthermore, even assuming *arguendo* that the Examiner's argument is correct, the above-mentioned limitation still is not taught or suggested because Balandrin does not teach or suggest that the convulsive disorder is selected from the group consisting of simple partial seizures, complex partial seizures, generalized tonic-clonic seizures, secondarily generalized seizures, status epilepticus, and trauma-induced seizures.

The Examiner also states that Balandrin teaches the administration of isovaleramide to hyperexcitable children, premenstrual patients, and substance abuse patients and relies on this teaching as evidence of isovaleramide's anticonvulsive behavior. *Id.* at p. 3. However, nothing in Balandrin supports the assertion that hyperexcitable children, premenstrual patients, or substance abuse patients have a convulsive disorder selected from the group consisting of simple partial seizures, complex partial seizures, generalized tonic-clonic seizures, secondarily generalized seizures, status epilepticus, and trauma-induced seizures. As such, the Examiner's

reliance on isovaleramide being administered to these patients provides no evidence of isovaleramide's anticonvulsive behavior.

The cited references also do not provide a reasonable expectation of success. One of ordinary skill in the art would not reasonably expect to treat the recited convulsive disorders by administering isovaleramide to a patient because nothing in the cited references, when combined, provides any teaching or suggestion that isovaleramide would have activity against the recited convulsive disorders. In addition, there is no reasonable expectation of success because Balandrin explicitly teaches that the properties of active components of a valerian extract, such as isovaleramide, are unpredictable.

In addition, the cited references do not provide a motivation to combine to produce the claimed invention. To provide a motivation or suggestion to combine, the prior art or the knowledge of a person of ordinary skill in the art must "suggest the desirability of the combination" or provide "an objective reason to combine the teachings of the references." M.P.E.P. § 2143.01. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *Id.* (emphasis in original). Applicants respectfully submit that nothing in the cited references, when combined, suggests the desirability of the combination or provides an objective reason to combine. Specifically, nothing in Balandrin suggests the desirability of, or provides an objective reason for, administering isovaleramide to a patient to treat a convulsive disorder, let alone a convulsive disorder selected from the group consisting of simple partial seizures, complex partial seizures, generalized tonic-clonic seizures, secondarily generalized seizures, status epilepticus, and trauma-induced seizures. Dorland also does not suggest the desirability of, or provide an objective reason for, administering isovaleramide to a patient to treat the recited convulsive disorders. Instead, as acknowledged by the Examiner, Dorland "show[s] the general meaning of the term 'convulsion' in the art." Office Action of April 28, 2005, p. 4.

Furthermore, Balandrin teaches away from combination with Dorland to produce the claimed invention because Balandrin explicitly teaches that isovaleramide has no anticonvulsant properties. See, Balandrin at column 4, lines 60-65. As such, a person of ordinary skill in the art at the time of the invention, after reading Balandrin and Dorland, would not have been motivated to administer isovaleramide to treat a convulsive disorder.

Since the cited references do not teach or suggest all of the claim limitations, do not provide a reasonable expectation of success, and do not provide a motivation to produce the claimed invention, the obviousness rejection of claim 37 is improper and should be withdrawn.

Obviousness Rejection Based on Balandrin in view of Dorland and J. Neurol. Neurosurg. Psychiatry, 50(9):1148-1152 (1987) to Schon *et al.*

Claim 39 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Balandrin in view of Dorland and the Abstract of J. Neurol. Neurosurg. Psychiatry, 50(9):1148-1152 (1987) to Schon *et al.* ("Schon"). Applicants respectfully traverse this rejection, as hereinafter set forth.

The obviousness rejection of claim 39 is improper because the cited references do not teach or suggest all of the claim limitations and do not provide a motivation to combine to produce the claimed invention.

The teachings of Balandrin and Dorland are as previously described.

The Abstract of Schon teaches that a majority of epileptic patients suffer from headaches, such as migraine headaches, after a seizure. Schon is limited to teaching this correlation between headaches and a seizure. Schon is silent about any treatment alternatives for the headaches.

As amended, claim 39 recites a method of treating headaches in a patient. The method comprises administering an effective amount of isovaleramide to a patient suffering from a headache.

The cited references do not teach or suggest all of the limitations of claim 39 because Balandrin, Dorland, and Schon, when combined, do not teach or suggest "administering an effective amount of isovaleramide to a patient suffering from a headache." Balandrin does not teach or suggest this limitation because Balandrin teaches administering isovaleramide as an anxiolytic or sedative. Nothing in Balandrin provides any teaching or suggestion that isovaleramide is useful to treat a headache. Dorland also does not teach or suggest this limitation because Dorland merely teaches a definition of the term "convulsion." Finally, Schon does not teach or suggest this limitation because, as acknowledged by the Examiner, "Schon et al is merely used to show that headaches of migraine type are common among patients who experience a convulsive attack." Office Action of April 28, 2005, p. 5. Applicants respectfully submit that nothing in Schon teaches or suggests a treatment for the headaches and, therefore,

Schon does not teach or suggest administering an effective amount of isovaleramide to a patient suffering from a headache. Rather, Schon only provides statistics on the incidence of headaches in epileptic patients.

The cited references also do not provide a motivation to combine to produce the claimed invention. Nothing in Balandrin, Dorland, and Schon, when combined, suggests the desirability of, or provides an objective reason for, administering an effective amount of isovaleramide to a patient suffering from a headache.

Since the cited references do not teach or suggest all of the claim limitations and do not provide a motivation to produce the claimed invention, the obviousness rejection of claim 39 is improper and should be withdrawn.

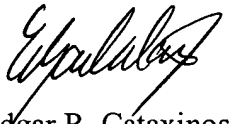
ENTRY OF AMENDMENTS

The amendments to claims 37 and 39 should be entered by the Examiner because the amendments are supported by the as-filed specification and drawings and do not add new matter.

CONCLUSION

Claims 37 and 39 are believed to be in condition for allowance, and an early notice thereof is respectfully solicited. Should the Examiner determine that additional issues remain that might be resolved by a telephone conference, the Examiner is respectfully invited to contact Applicants' undersigned attorney.

Respectfully submitted,



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